PROGRESS REPORT ON NASA RESEARCH GRANT NGR-05-035-003 FOR THE PERIOD 1 DECEMBER 1966 THROUGH 31 MARCH 1967. "STUDY OF BODY ENERGY CONSERVATION, EMPHASIZING SPACE FLIGHT ENVIRONMENTAL EFFECTS ON ORGANISMS"

During this report period numerous attempts were made to induce hibernation in the fattened ground squirrels using first a freezer regulated at 5° C and secondly a refrigerator regulated at 7° C. For reasons unknown hibernation was not achieved. Possible explanations are (a) noise from the compressor-motor and (b) disturbance due to opening of the freezer or refrigerator daily in order to replenish the air supply. A number of the squirrels died and the remainder are to be used in studies with radioactive substrates similar to those described below for rats.

In order to supplement the enzyme studies made on adipose tissue from ground squirrels and rats as reported previously, the metabolism of acetate-2-C^{14} by liver of rats has been studied in the presence of various nonlabelled metabolites at incubation temperatures of 37°, 27°, 17° and 7° C. The nonlabelled metabolites used were glucose, fructose, pyruvate, succinate and glycine. These substances were chosen in order to provide information on the site of inhibition of acetate metabolism as the temperature was lowered and oxidation processes slowed.

Conversion of acetate C^{14} to fatty acid-C^{14}, cholesterol-C^{14}, $C^{14}O_2$ and total lipid-C^{14} was studied. At 37° glucose and fructose were essentially without effect on conversion of acetate to total lipid C^{14}, whereas pyruvate, succinate and glycine reduced the conversion by almost 50 per cent. At 27° total lipid C^{14} was about one-third that at 37° in the presence of glucose whereas in the presence of fructose, pyruvate, succinate or glycine the total lipid C^{14} values were only about one-sixth those at 37°. At 17° total lipid C^{14} values in all cases were about 5% of the values at 37° and at 7° C no lipid C^{14} could be detected. Thus, it would appear (1) that at hibernating temperatures (5-7°) rat liver is unable to synthesize lipids, (2) at 17° C the synthesis rate is very low, and (3) at 27° fructose is apparently metabolized more readily than glucose since conversion of acetate to lipid-C^{14} in the presence of fructose is only one-fifth that when glucose is present. Similar findings were noted for total fatty acid-C^{14} and for cholesterol-C^{14}.

With regard to acetate-C^{14} oxidation to $C^{14}O_2$ at 37°, addition of glucose, fructose or glycine had essentially no effect on acetate oxidation, whereas in the presence of pyruvate or succinate, oxidation was reduced by more than 50%. At 27° glucose addition still had no effect, but fructose, pyruvate, succinate and glycine reduced oxidation by 50, 80, 80 and 25%, respectively, below control values. Even at 17° C glucose addition did

not influence acetate oxidation -- which was essentially the same as at 37° or 27° -- whereas addition of the other metabolites, except glycine, markedly inhibited acetate oxidation. At 7° C essentially no acetate oxidation occurred in any condition. It may be concluded that (1) conversion of acetate to $C^{14}O_2$ is affected less by reduced temperature than is its conversion to lipid-C^{14}, (2) neither glucose nor glycine are well metabolized at 17° C, and (3) at 7° metabolic processes in rat liver slices is essentially nil.

It would appear that 17° C is about the lowest temperature at which synthetic and oxidative processes can be maintained in rat tissue in vitro. Whether this is true for the intact rat will be determined by future studies. Similar studies will be carried out on tissues of the ground squirrel.

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